

## Original Article

# Response to phenylephrine testing in upper eyelids with ptosis

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## Abstract

**Objective**—To evaluate the response of ptotic upper eyelids to topical phenylephrine 10%.

**Methods**—The medical records of patients referred for ptosis evaluation over an 18-month period were retrospectively reviewed. Seventy-seven ptotic upper eyelids with aponeurotic dehiscence in 47 patients were given 1 drop of 10% phenylephrine. Margin-to-reflex distance 1 (MRD1) and levator excursion were recorded and photography of lid height was performed both pre- and 5 minutes post-phenylephrine testing.

**Results**—A total of 77 ptotic upper eyelids of 47 patients were included. In 22% of lids, phenylephrine testing produced no response; in 18%, lid elevation of 0.5–1 mm; in 35%, elevation of 1.5–2 mm; and in 25%, elevation of > 2 mm. Subgroup analyses revealed a higher proportion of response in cases of mild to moderate ptosis compared with cases of severe ptosis. The amount of levator function in these cases of aponeurotic dehiscence did not correlate with the amount of response to phenylephrine.

**Conclusions**—A majority of ptotic eyelids, regardless of levator function, responded to topical phenylephrine, which has been demonstrated to be necessary for successful Müller's muscle resection ptosis repair. While the severity of ptosis was linked to eyelid response to phenylephrine, the degree of levator function did not appear to affect an eyelid's response to phenylephrine. In this study cohort, phenylephrine was shown to stimulate Müller's muscle contraction independently of levator function.

Blepharoptosis is among the most commonly encountered eyelid disorders in ophthalmology. Multiple surgical options exist for its treatment, including Müller's muscle resection (MMR), first introduced by Putterman and Urist in 1975 as a modification of the Fasanella-Servat procedure.<sup>1,2</sup> It is well documented that preoperative response to topical phenylephrine is an important criterion for successful MMR ptosis repair.<sup>1,3–7</sup> During phenylephrine testing, exposure to topical phenylephrine, an alpha adrenergic agonist, contracts the sympathetically innervated Müller's muscle and elevates the lid. Studies have shown that maximal results from Müller's muscle resection are seen in patients with both good response to phenylephrine testing and good levator function.<sup>8</sup> The sympathomimetic effect of phenylephrine theoretically involves only the action of Müller's muscle, so it is curious that levator function also affects the

outcome of Müller's muscle resection. This may be attributable to the probability that Müllerectomy also includes some degree of plication of the posterior aspect of the levator aponeurosis.<sup>8,9</sup> To our knowledge, the present study is the first to evaluate the response to topical phenylephrine testing in upper eyelids with aponeurotic ptosis with various degrees of levator excursion and to describe the proportion of responders and quantify the response.

## Subjects and Methods

The medical records of all patients with aponeurotic dehiscence referred to one author (SKF) for ptosis evaluation over an 18-month period, from January 2006 to June 2007, were retrospectively reviewed. These patients were subdivided into different ptosis etiologies

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including age-related, postoperative, and contact lens-related ptosis. Some patients had multifactorial contributions to their aponeurotic ptosis and thus were incorporated into more than one subcategory. For example, an elderly patient with bilateral age-related levator dehiscence ptosis had worse ptosis on one side after cataract surgery: one lid was categorized as age-related aponeurotic ptosis and the contralateral lid was categorized as both age-related and postoperative aponeurotic ptosis. Patients with no other attributable cause for ptosis and no evidence of associated neuropathy or myopathy were determined to have aponeurotic ptosis and were included. Specifically, patients with trauma to the eyelid, cranial nerve palsies, tumors causing mechanical ptosis, congenital ptosis, and Horner's syndrome were excluded. This study was conducted under the auspices of the Boston University and Massachusetts Eye and Ear Institutional Review Board, in compliance with the rules and regulations of the US Health Insurance Portability and Accountability Act of 1996 and in adherence to all other relevant federal and state laws.

In the phenylephrine test, 1 drop of phenylephrine 10% solution was placed at the superior limbus of each eye with a ptotic eyelid.<sup>1</sup> The drop was placed with the eye in downgaze, with the examiner's finger elevating the upper eyelid. Margin-to-reflex distance 1 (MRD1) was recorded by the author and photography was performed both before and 5 minutes after phenylephrine testing. MRD1 was measured by one author (SKF) by assessing the distance between the pupillary light reflex from a muscle light to the margin of the upper eyelid using a millimeter ruler held adjacent to the patient's lateral canthus. A finger was placed over the patient's brow to ensure frontalis relaxation. Two observers reviewed the photographs to determine MRD1 pre- and post-phenylephrine placement. Clinical measurements and photographic determinations were compared and in all cases were within 1 mm of each other. If there was a discrepancy, the mean of the two measurements was used. Clinical measurements of levator function involved the examiner stabilizing the patient's frontalis muscle with a finger placed above the brow while the patient looked from far downgaze to far upgaze. The patient's age, sex, prior ocular history, cause of ptosis, severity of ptosis, levator function, and response to phenylephrine were recorded. Severity of ptosis was categorized as follows: mild ptosis, MRD1 of 2–3 mm; moderate ptosis, MRD1 of 0.5–1.5 mm; and severe ptosis, MRD1 of  $\leq 0$  mm.

### Data Analysis

Response to phenylephrine was defined as the change in MRD1, where  $\Delta$ MRD1 is equal to post-phenylephrine

**Table 1.** Overall response to phenylephrine ( $\Delta$ MRD1) in millimeters

Response	Number (%)
$\Delta$ MRD1 = 0mm	17/77 (22.1)
0.5 mm $\geq$ $\Delta$ MRD1 $\geq$ 1 mm	14/77 (18.2)
1.5 mm $\geq$ $\Delta$ MRD1 $\geq$ 2 mm	27/77 (35.1)
$\Delta$ MRD1 > 2 mm	19/77 (24.7)

MRD1, margin-to-reflex distance 1.

MRD1 minus pre-phenylephrine MRD1. The  $\Delta$ MRD1 was categorized as follows: zero, 0.5–1 mm, 1.5–2 mm, and >2 mm. Additional analyses compared response to phenylephrine with severity of ptosis, etiology of levator dehiscence, and levator function. Statistical significance of the difference in the  $\Delta$ MRD1 within subgroups (etiology of ptosis, severity of ptosis, levator function) was analyzed using the Kruskal-Wallis nonparametric analysis of variance (ANOVA) test.

### Results

A total of 47 patients (23 males [49%]) with 77 ptotic upper eyelids were evaluated. All patients had ptosis due to aponeurotic dehiscence. Mean patient age with standard deviation was  $67.1 \pm 17.1$  years (range, 15–86 years)

Of the 77 ptotic lids, 70 (91%) were due to age-related changes, 26 (34%) had a history of intraocular surgery, and 4 (5%) were attributable to contact lens wear. Of the 77 ptotic lids, 20 (26%) were categorized as a combination of age-related and postoperative, and 3 were a combination of age-related and contact lens wear.

Of the 77 eyelids, 13 (17%) had mild ptosis; 39 (51%), moderate ptosis; and 25 (33%), severe ptosis. Seventeen eyelids (22%) had a  $\Delta$ MRD1 of 0 mm; 14 (18%), a  $\Delta$ MRD1 of 0.5–1 mm; 27 (35%), a  $\Delta$ MRD1 of 1.5–2 mm; and 19 (25%), a  $\Delta$ MRD1 of >2 mm (Table 1).

Response to phenylephrine was analyzed for each severity subgroup (Figure 1). Of 13 eyelids with mild ptosis, 12 (92%) had some response to phenylephrine. Of 39 eyelids with moderate ptosis, 31 (80%) had some response to phenylephrine. However, of 25 eyelids with severe ptosis, 17 (68%) had some response to phenylephrine. The difference in response across ptosis severity subgroups was not statistically significant ( $P = 0.734$ ). Response to phenylephrine was also analyzed for ptosis etiology subgroups (Figure 2). Eyelids with age-related aponeurotic ptosis were compared with lids with postoperative and contact lens-related ptosis. Of lids with postoperative ptosis, 77% had at least 1.5 mm of elevation. On the other hand, among eyelids without sur-

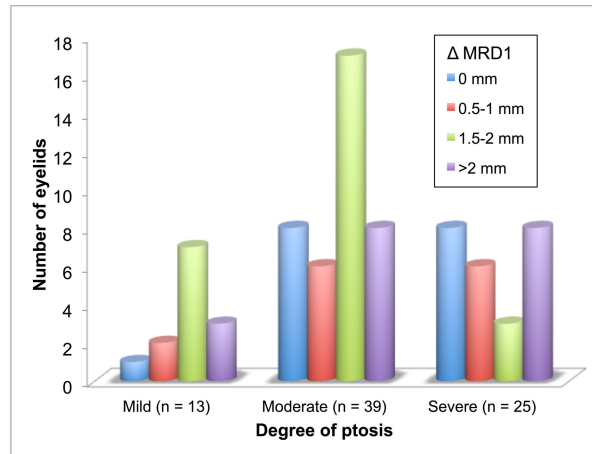


Figure 1. Response to phenylephrine (Δ margin reflex distance 1 [MRD1]) by severity of ptosis.

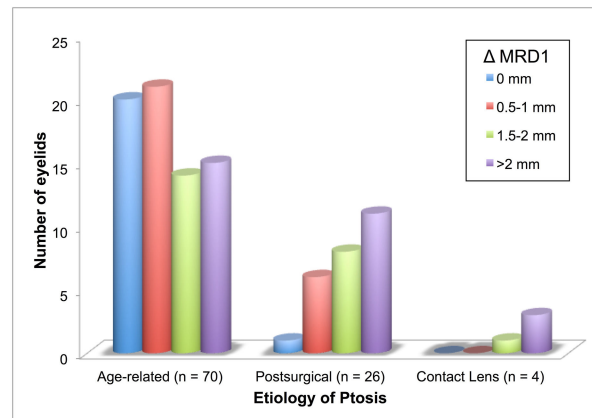


Figure 2. Response to phenylephrine (ΔMRD1): ptosis etiology subgroup analysis.

gery and only age-related changes, 42% had at least 1.5 mm of elevation. There were only 4 eyelids with contact lens-involving ptosis. All 4 had at least 1.5 mm of elevation. The difference between these three groups was statistically significant ( $P = 0.012$ ) Finally, response to phenylephrine was analyzed for varying amounts of levator function. Eyelids were classified under three categories of levator function: excellent levator function ( $\geq 15$  mm of excursion), good levator function (11–14 mm of excursion), and fair levator function ( $\leq 10$  mm of excursion). Forty-three of eyelids (56%) had excellent levator function; 36%, good levator function; and 8%, poor levator function (Table 2).

Among eyelids with excellent or good levator function, 80% had some response to phenylephrine and 61% had at least 1.5 mm of response to phenylephrine. Of the 6 eyelids with fair levator function, 50% did not respond

Table 2. Levator function (N = 47 patients, 77 eyelids)

Function	Number (%)
Excellent ( $\geq 15$ mm)	43/77 (55.8)
Good (11 mm to 14 mm)	28/77 (36.4)
Fair ( $\leq 10$ mm)	6/77 (7.8)

at all to phenylephrine (Figure 3). The difference in response to phenylephrine across levator function groups was not statistically significant ( $P = 0.768$ ).

No adverse effects from phenylephrine testing were noted in any patients in this study.

## Discussion

That response to topical phenylephrine is necessary for a successful outcome in Müller’s muscle resection ptosis

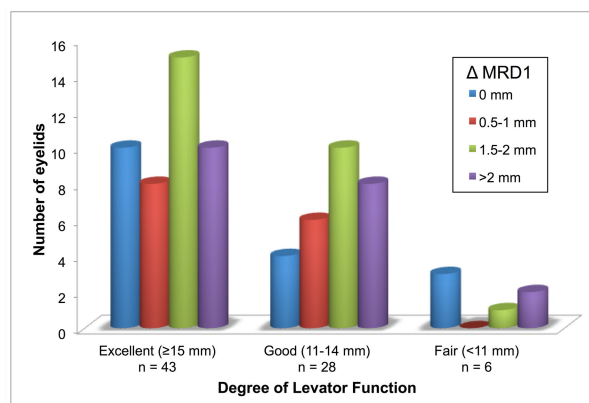


Figure 3. Response to phenylephrine ( $\Delta$ MRD1): levator function subgroup analysis.

repair has been well documented.<sup>1,2</sup> During phenylephrine testing, the sympathetically innervated Müller's muscle contracts and elevates the lid when exposed to topical phenylephrine, an alpha-adrenergic agonist. We are unaware of previous studies addressing the question of what proportion of ptotic eyelids with aponeurotic dehiscence respond to topical phenylephrine and whether there are any predictive factors, such as severity of ptosis, amount of levator function, or history of prior intraocular surgery.

Overall, 78% of eyelids in this study had some response to phenylephrine, and 60% responded  $\geq 1.5$  mm. Thus more than half of the eyelids tested had enough response to be considered candidates for Müller's muscle resection surgery.

Lids with mild ptosis had a phenylephrine response rate of 88%, with 69% responding  $\geq 1.5$  mm. These lids with mild ptosis are often considered to be the best candidates for Müller's muscle resection surgery, because this technique usually will not raise the lid more than 2 mm.<sup>1,4,5</sup> Thirty-two percent of eyelids with severe ptosis did not respond to phenylephrine testing. However, the same percentage of severely ptotic eyelids (32%) responded exuberantly (2.5–3.5 mm) to phenylephrine testing. Investigation of the demographics, etiology of ptosis, and the degree of levator function within this subgroup of severe ptosis showed no correlation with the response to phenylephrine. Thus, there may still be a role for attempting phenylephrine testing on patients with severe ptosis and considering conjunctival Müller's muscle resection based on these findings.

Ninety-six percent of eyelids in postoperative eyes responded to phenylephrine testing. Additionally, all eyelids (4/4) with contact lens–related ptosis had at least

1.5 mm response to phenylephrine, including 2 with severe ptosis. The difference in response seen between these groups was statistically significant. It has been postulated that cataract surgery contributes to the onset of ptosis due to the stretch of the levator from the speculum countering the strength of the orbicularis. However, manipulation of the upper eyelid when placing postoperative eyedrops may also contribute to the development of ptosis, as when the upper eyelid is stretched when placing a contact lens.<sup>10</sup>

A majority of the eyelids (92%) had ptosis with good or excellent levator excursion. There was no statistically significant difference between the degree of levator function compared to the amount of response to phenylephrine. Georgescu et al showed that in 4 eyelids with fair levator function (4–8 mm) and satisfactory response to phenylephrine, they were able to achieve a good result (mean MRD1, 3.38) after conjunctival Müller's muscle resection.<sup>11</sup> Thus indiscriminate of levator function, the response to phenylephrine may be the most predictive element for a successful Müller's muscle resection.

These trends in phenylephrine response may help surgeons anticipate which patients are likely to benefit from preoperative phenylephrine testing. This can save time in the clinic and may help avoid the risk, albeit low, of adverse events, which have been reported with topical phenylephrine testing, including hypertension exacerbation and cardiac arrest.<sup>12</sup> Thus, avoidance of testing on a subgroup of patients with a cardiac history, such as supraventricular tachycardia or volatile hypertension, should be considered.

There has been some discrepancy regarding the technique of phenylephrine drop placement. According to Put-

terman's publications, the drop was placed between the superior globe and the upper eyelid, aiming toward the superior fornix<sup>1</sup>; however, other accounts, including Ben Simon et al describe a technique of instilling the drop in the inferior fornix.<sup>13</sup> Whatever the location of the drop placement, we felt that placement anywhere along the ocular surface would have the same effect on the upper eyelid.

We conclude, based on our retrospective study, that pre-operative phenylephrine testing in upper eyelid ptosis has a greater response rate and greater amount of lid elevation in patients with mild ptosis and patients with ptosis secondary to prior intraocular surgery. Patients with severe ptosis had a lower response rate to phenylephrine testing and may be poorer candidates for Müller's muscle resection ptosis repair; however, we also found that it is possible to elicit 2.5–3.5 mm of response in patients with severe ptosis, which may influence a surgeon's decision to perform a Müller's muscle resection. Moreover, patients with lower than normal levator excursion may still be candidates for Müller's muscle resection in light of the response to phenylephrine observed in our study.

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